UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/646,633	08/22/2003	Elizabeth S. Light	03-776-D	9782

20306 7590 05/24/2006

MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP
300 S. WACKER DRIVE
32ND FLOOR
CHICAGO, IL 60606

EXAMINER	
SWITZER, JULIET CAROLINE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 05/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/646,633	LIGHT ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*; 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *1-7 and 17-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-7 and 17-22, drawn to reagents for detecting HPV and kits comprising the same, classified in class 536, subclass 23.1.

II. Claims 8-16, drawn to methods for detecting HPV, classified in class 435, subclass 6.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the products of invention I can be sued for different methods, for example to express polypeptides encoded within the HPV genome or for nucleic acid purification.

3. Because these inventions are independent or distinct for the reasons given above and have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

4. Because these inventions are independent or distinct for the reasons given above and the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

5. During a telephone conversation with Donald Zuhn on 3/23/06 a provisional election was made with traverse to prosecute the invention of group II, claims 8-16. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-7 and 17-22 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Dependency

7. It is noted that claims 8-16 all depend from non-elected claim 1. Prior to allowance of any of claims 8-16 they will be required to be amended so that they do not depend from non-elected claims.

8. Claim 14 appears to have a typographical error when it recited "the reagent consisting essential of DNA probes..." and would be corrected if it recited "the reagent consists essential of DNA probes...."

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 8-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejected claims are indefinite because they depend from claim 1, which is indefinite over the recitation of "capable of specifically hybridizing" because capability is a latent characteristic and the claims do not set forth the criteria by which to determine capability. That is, it is not clear whether the recited probes have the potential to specifically hybridize or do in fact hybridize to the high-risk HPV DNA. Amendment of the claim to read, for example, "which hybridize" would obviate this rejection.

The claims are further indefinite over the recitation of "high-risk HPV DNA" and "low-risk HPV DNA" in claim 1 because the claims do not set forth the standards by which to determine the relative risk level of a particular HPV DNA. That is, there is no art established clear standard for the determination of which HPV DNA is "high" versus "low" risk DNA. For example, the instant claims include HPV types 31, 33, and 51 as "high risk" types, while these types are also known in the literature as "medium" risk HPV types (see Gomez *et al.* Eur. J. Histochem., Vol. 36, pages 137-142, 1992, p. 141, last sentence first paragraph). Thus, in light of the lack of a clear definition of high versus low risk HPV types is not possible to know from the claims which do not recite particular HPV types which types are considered "high" risk within the scope of the claims and which are considered "low" risk.

Claim 15 is indefinite because the claim recites that the probes are present in recited "amounts" but then lists a series of percentages for each probe. The claim does not set forth

what the percentages are portions of (i.e. total hybridization mix, probe mix, etc), and it does not set forth how the percentages represent particular amounts.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims are drawn to methods for detecting human papilloma virus DNA in a cell sample, and requires the use of reagents which comprise a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Dependent claims included in the rejection recite particular HPV types which hybridize to the probes and particular probes which do not, recite that the probes are "full length," and include specific concentrations of particular probes in the reagent. The claims do not set forth any particular sequences or structure for the probes, and in fact only identify the claimed nucleic acids in terms of their function. The genus of the claimed reagents, therefore, includes any probe which is specific to any HPV type that is known to cause cancer, a genus which includes hundreds of thousands of possible reagents. Even for claims which recite particular HPV types, these claims encompass any set of oligonucleotide probes which would hybridize specifically to the recited types. The claims which recite "full length" probes are themselves quite broad, since the

definition of "full length" in the specification is inclusive of "sequence variations and shortening of the probe length (specification page 5)." From applicant's specification, Applicant appears to be in possession of a single probe combination which meets the functional limitations of the instant claims, that is a probe set that comprises probes that were produced by nick-translation of the full length genome of six separate plasmids, with one plasmid containing the whole genome of a HPV type and the six types being 16, 18, 31, 33, 35, and 51, wherein types 18, 33, 25, and 51 are present at 0.5 nanograms per milliliter of solution and types 16 and 31 re present at 0.2 nanograms per milliliter of solution (see p. 13, example 3), since this is the only reagent demonstrated by applicant to specifically hybridize only to those "high risk" types of HPV designated by Applicant, and not to "low risk" HPV, see Table 5. Thus, applicant has express possession of only one species in a genus which comprises hundreds of millions of different possibilities.

With regard to the written description, all of these claims encompass reagents comprising nucleic acid sequence different from those disclosed in the specific reagents which for which no written description is provided in the specification.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only a single reagent meeting the functional limitations of the claims is described, yet hundreds of thousands of possible reagents are encompassed by the

claims. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of reagents modified from the single example given but possessing the functional characteristics required by the claims.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 8, 9, 10, 11, 12, 13, and 14 are rejected under 35 U.S.C. 102(a) as being anticipated by Nuovo et al. (June 1998 Diagnostic Molecular Pathology 7(3): 158-163).

Nuovo et al. a method which comprises a step of adding a reagent that comprises a consensus probe cocktail that contains "multiple high HPV types" (page 160) and that detectably hybridizes to high risk HPV types 16/18, 31, 33, 35, and 51, as well as to HPV types 39, 45, 52, 56, 58, 59, 68, and 70, but not to any of the low risk types tested (see Table 2), and detecting the presence or absence of hybridization inside cells in the sample, thus teaching the limitations of claims 8-10. Regarding claims 11 and 12, Nuovo et al. teach treatment with

proteases pepsin and proteinase K, which is a means of deparafinning a cell sample (p. 159). Regarding claim 14, the reagent is considered to comprise probes to these types since it detects these types.

14. Claims 8, 10, 11, 12, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Nuovo et al. (The Journal of Histotechnology, Vol. 18, No. 2, June 1995).

Nuovo et al. teach methods which include in situ hybridization of cocktails of HPV genomic probes to cervical cell samples (p. 105-106). Nuovo et al. teach the use of a mixture of probes for HPV 16 and 18 and a separate mixture of probes HPV 31, 33, and 35. These are all considered "high risk" HPV types. Further, Nuovo et al. teach hybridization with individual HPV probes for types 16, 18, 21, 22 and 35. These probe reagents each by themselves is a "plurality" of DNA probes (because they are comprisesd of multiple molecules of DNA probe" capable of specifically hybridizing high-risk HPV DNA. Nuovo et al. teach that the probes taught by Digene are made using the entire genome (p. 106).

Thus, Nuovo et al. provide a method which comprises the steps of (a) adding a reagent which comprise a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not to low-risk HPV DNA to a cell sample and (b) detecting the presence or absence of hybridization inside cells in the cell sample (p. 106, In Situ Hybridization).

Regarding claim 10, Nuovo et al. teach that low stringency hybridization conditions are used (p. 106). The probe set taught by Nuovo et al. which comprises full length genomic probes to HPV types 16 and 18 would be expected to exhibit some hybridization to each of the HPV types recited in claim 10 under low stringency conditions. This is evidenced by the instant

specification which demonstrates in Table 1 that these two probes are "capable of" cross-hybridizing to these types.

Regarding claim 11, Nuovo et al. teach pretreating with the protease trypsin (p. 106).

Regarding claim 12, Nuovo et al. teach deparaffining the cell sample (p. 106).

Regarding claim 13, Nuovo et al. teach that the reagents contains full-length HPV probes.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 9 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nuovo et al. in view of Cox et al. (American Journal of Obstet. Gynecol. March 1995, pages 946-954).

Nuovo et al. teach methods which include in situ hybridization of cocktails of HPV genomic probes to cervical cell samples (p. 105-106). Nuovo et al. teach the use of a mixture of probes for HPV 16 and 18 and a separate mixture of probes HPV 31, 33, and 35. These are all

considered "high risk" HPV types. Further, Nuovo et al. teach hybridization with individual HPV probes for types 16, 18, 21, 22 and 35. These probe reagents each by themselves is a "plurality" of DNA probes (because they are comprisesd of multiple molecules of DNA probe" capable of specifically hybridizing high-risk HPV DNA. Nuovo et al. teach that the probes taught by Digene are made using the entire genome (p. 106). Nuovo et al. teach additional probes to individual, including a probe to HPV (p. 106).

Thus, Nuovo et al. provide a method which comprises the steps of (a) adding a reagent which comprise a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not to low-risk HPV DNA to a cell sample and (b) detecting the presence or absence of hybridization inside cells in the cell sample (p. 106, In Situ Hybridization).

Regarding the limitation of claim 9, Nuovo et al. do not teach a method which uses a reagent that hybridizes to types 16, 18, 31, 33, 35, and 51 but not those listed in the claims, and Nuovo et al. does not teach a reagent which consists essentially of DNA probes to HPV types 16, 18, 31, 33, 35, and 51.

Cox et al. teach methods for detection of HPV in clinical samples which utilize a cocktail of common cancer-associated high-risk HPV types, including probes that hybridize to all of those required for hybridization in claim 9, but none of those recited for hybridization in claim 9, and additionally comprising all of the probes recited in claim 14.

It would have been prima facie obvious to one of ordinary skill in the art to have modified the probe set taught by Nuovo et al. so as to have provided a comprehensive "high-risk" cocktail for use in the methods taught by Nuovo et al., similar to the one exemplified by Cox et al. One would have been motivated to combine the "high risk" probes taught by Nuovo

et al. in order to have provided a method for detection of high risk HPV types that can be used in the sensitive in situ hybridization methods taught by Nuovo et al., but which could detect in a single hybridization assay a wider variety of high-risk HPV types. One would have been further motivated by the teachings of Cox et al. which exemplify such a cocktail, albeit for use in a different method. Thus, in light of the teachings of the prior art, the claimed invention is prima facie obvious.

18. Claims 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nuovo et al. in view of Cox et al. as applied to claims 9 and 14 above, and further in view of view of Bauer *et al.* (US 5639871).

The teachings of Nuovo et al. in view of Cox et al. are applied to this rejection as they were applied in the previous rejection.

Nuovo et al. in view of Cox et al. do not provide the particular concentrations or amounts of each particular strain of HPV probe requied in the cocktail.

However, the optimization of hybridization assays by determining ideal probe concentrations was routine in the prior art at the time the invention was made, as is exemplified by Bauer *et al.* who teach "The optimal ration and concentration of probe fragments to be used in the hybridization are determined empirically (Col. 51, lines 60-63)."

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have experimented with different probe concentrations so as to arrive at an optimal concentration for the detection of HPV in a sample. It is well settled that routine optimization is not patentable, even if it results in significant improvements over the

prior art. In support of this position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955):

> Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. In re Dreyfus, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52 ; In re Waite et al., 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586 . Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. In re Swenson et al., 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372 ; In re Scherl, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204 . However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. In re Sola, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433 ; In re Normann et al., 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308 ; In re Irmscher, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314 . More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Swain et al., 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412 ; Minnesota Mining and Mfg. Co. v. Coe, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213 ; Allen et al. v. Coe, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

For these reasons, the claimed invention is *prima facie* obvious.

Conclusion

19. No claims are allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday, Tuesday, or Thursday, from 9:00 AM until 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached by calling (571) 272-0735.

The fax phone numbers for the organization where this application or proceeding is

assigned are (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Juliet C. Switzer
Primary Examiner
Art Unit 1634

May 11, 2006